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ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: COMBINATION OF A PDE IV INHIBITOR AND A TNF-ALPHA ANTAGONIST

(57) Abstract: The subject invention relates to therapeutic combinations and methods for the treatment of inflammatory conditions and diseases. Particularly the present invention relates to treatments and methods for PDE IV-related conditions and for TNF-alpha-related conditions using a combination of a PDE IV inhibitor and a TNF-alpha antagonist.

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## INTERNATIONAL SEARCH REPORT

International Application No

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/52 A61K31/517 A61K31/573 A61K31/55 A61K31/522  
 A61K31/00 A61P11/06 A61P11/08

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 03/039548 A (MERCK PATENT GMBH ; BEIER NORBERT (DE); EHRING THOMAS (DE); WOLF MICHA) 15 May 2003 (2003-05-15) claims 11-13,18	1,2,5-8, 12-15
X	WO 98/41232 A (BASF AG ; CARTER ADAM (US); SEKUT LES (US); GHAYUR TARIQ (US); TRACEY) 24 September 1998 (1998-09-24) page 68, paragraph 2; claims 1,9,17,20,23; examples 8,9	1-5, 8-12,15
X	WO 02/060896 A (CHAMBERS ROBERT JAMES ; MAGEE THOMAS VICTOR (US); MARFAT ANTHONY (US);) 8 August 2002 (2002-08-08) page 1, paragraphs 1,4 page 2, paragraph 3 - page 27, paragraph 2 page 161, paragraph 2 - page 162, paragraph 2; claims 9,10	1,2,5-8, 12-15
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 416 248 A (VESTA MED PTY LTD) 13 March 1991 (1991-03-13) page 1, paragraph 1; claims 1-3; example 6 -----	1-4, 8-11,15
X	EP 0 670 163 A (RENTSCHLER ARZNEIMITTEL) 6 September 1995 (1995-09-06) column 2, lines 20-33; claims 1-3 -----	1-4, 8-11,15
X	DATABASE WPI Section Ch, Week 198618 Derwent Publications Ltd., London, GB; Class B02, AN 1986-055685 XP002284373 & JP 61 057516 A (SANDOZ SA) 24 March 1986 (1986-03-24) abstract -----	1-4, 8-11,15
X	DATABASE WPI Section Ch, Week 200317 Derwent Publications Ltd., London, GB; Class B04, AN 2003-168217 XP002284374 & CN 1 161 855 A (LUO L) 15 October 1997 (1997-10-15) abstract -----	1-4, 8-11,15
X	DATABASE WPI Section Ch, Week 199921 Derwent Publications Ltd., London, GB; Class B05, AN 1999-248440 XP002284375 & JP 11 071281 A (TAISHO PHARM CO LTD) 16 March 1999 (1999-03-16) abstract -----	1-4, 8-11,15
X	GB 2 163 957 A (SANDOZ LTD) 12 March 1986 (1986-03-12) claim 1.34; examples 1-4 -----	1-4, 8-11,15
Y	GOZZARD N ET AL: "EFFECT OF THE GLUCOCORTICOSTEROID BUDESONIDE AND A NOVEL PHOSPHODIESTERASE TYPE 4 INHIBITOR CDP840 ON ANTIGEN-INDUCED AIRWAY RESPONSES IN NEONATALLY IMMUNISED RABBITS" 1996, BRITISH JOURNAL OF PHARMACOLOGY, BASINGSTOKE, HANTS, GB, PAGE(S) 1201-1208 , XP009026550 ISSN: 0007-1188 abstract -----	1-15
	----- -/-	

## INTERNATIONAL SEARCH REPORT

International Application No

/IB2004/000616

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HATZELMANN ARMIN ET AL: "Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro" JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, vol. 297, no. 1, April 2001 (2001-04), pages 267-279, XP001024814 ISSN: 0022-3565 abstract	1-15
X	WILLIAMS R O ET AL: "Combination therapy with DMARDs and biological agents in collagen- induced arthritis" CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 1999 ITALY, vol. 17, no. 6 SUPPL. 18, 1999, pages S115-S120, XP009017873 ISSN: 0392-856X page 118, column 3, paragraph 3 - page 119, column 1, paragraph 2	1,2,6,9, 13,15

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/IB2004/000616

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03039548	A	15-05-2003	WO 03039548 A1	15-05-2003
WO 9841232	A	24-09-1998	US 6054487 A	25-04-2000
			AU 734756 B2	21-06-2001
			AU 6760498 A	12-10-1998
			BG 103808 A	31-07-2000
			BR 9810409 A	22-08-2000
			CA 2282845 A1	24-09-1998
			CN 1269722 T	11-10-2000
			DE 998300 T1	01-03-2001
			EP 0998300 A1	10-05-2000
			ES 2146192 T1	01-08-2000
			HU 0104439 A2	29-04-2002
			ID 22975 A	23-12-1999
			JP 2002504091 T	05-02-2002
			NO 994506 A	17-11-1999
			NZ 337769 A	27-09-2002
			PL 336464 A1	19-06-2000
			SI 20110 A	30-06-2000
			SK 122199 A3	11-12-2000
			TR 9902615 T2	21-03-2000
			WO 9841232 A2	24-09-1998
WO 02060896	A	08-08-2002	BR 0116845 A	25-02-2004
			CA 2436544 A1	08-08-2002
			EE 200300361 A	15-12-2003
			EP 1373258 A1	02-01-2004
			HU 0302891 A2	29-12-2003
			WO 02060896 A1	08-08-2002
			NO 20033399 A	25-09-2003
			US 2003027845 A1	06-02-2003
EP 0416248	A	13-03-1991	DE 69023989 D1	18-01-1996
			DE 69023989 T2	15-05-1996
			EP 0416248 A2	13-03-1991
			ZA 9005552 A	24-02-1993
EP 0670163	A	06-09-1995	DE 4332041 A1	23-03-1995
			CZ 9402300 A3	12-04-1995
			EP 0670163 A1	06-09-1995
			HU 70054 A2	28-09-1995
			JP 7247215 A	26-09-1995
			NO 943288 A	22-03-1995
			SK 111894 A3	10-05-1995
JP 61057516	A	24-03-1986	AU 4617185 A	20-02-1986
			BE 903065 A1	14-02-1986
			WO 8601108 A1	27-02-1986
			DD 238919 A5	10-09-1986
			DE 3528481 A1	27-02-1986
			DK 370085 A	17-02-1986
			FR 2569109 A1	21-02-1986
			GB 2163957 A	12-03-1986
			GR 851988 A1	10-12-1985
			HU 40568 A2	28-01-1987
			IT 1200102 B	05-01-1989
			LU 86044 A1	18-02-1986
			NL 8502178 A	17-03-1986

# INTERNATIONAL SEARCH REPORT

formation on patent family members

International Application No

/IB2004/000616

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 61057516 A		PT 80961 A , B SE 8503771 A ZA 8506247 A	01-09-1985 17-02-1986 25-03-1987
CN 1161855 A	15-10-1997	NONE	
JP 11071281 A	16-03-1999	NONE	
GB 2163957 A	12-03-1986	AU 4617185 A BE 903065 A1 WO 8601108 A1 DD 238919 A5 DE 3528481 A1 DK 370085 A FR 2569109 A1 GR 851988 A1 HU 40568 A2 IT 1200102 B JP 61057516 A LU 86044 A1 NL 8502178 A PT 80961 A , B SE 8503771 A ZA 8506247 A	20-02-1986 14-02-1986 27-02-1986 10-09-1986 27-02-1986 17-02-1986 21-02-1986 10-12-1985 28-01-1987 05-01-1989 24-03-1986 18-02-1986 17-03-1986 01-09-1985 17-02-1986 25-03-1987